

Primary Osteosarcoma of the Urinary Bladder Metastatic to Lung

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Abstract

Extra-skeletal osteosarcoma (ESOS) is a rare neoplasm that represents less than 2% of all soft tissue sarcomas. Common reported sites of involvement include limbs, retroperitoneum, chest wall and buttocks. ESOS arising primarily in parenchymatous organs are extremely uncommon, with the involvement of the urinary bladder is even rarer. We herein report a case of primary ESOS of the urinary bladder in a 48 year-old male patient.

Keywords: Urinary bladder; Osteosarcoma; Bone forming tumors; Lung metastases; SATB2

Introduction

Extra-skeletal osteosarcoma (ESOS) is a rare neoplasm that represents less than 2% of all soft tissue sarcomas [1]. Common reported sites of involvement include limbs, retroperitoneum, chest wall and buttocks [2]. ESOS arising in parenchymatous organs is extremely uncommon [3], with the primary involvement of the urinary bladder even rarer [4]. We herein report a case of primary ESOS of the urinary bladder in a 48-year-old male patient.

Case Report

A 48-year-old male patient presented to our hospital with his-

tory of hematuria for 3 days. An abdominal ultrasound was performed and revealed a urinary bladder right anterolateral polypoid soft tissue endo-luminal fungating mass 5 × 6 cm, with central echogenic part and peripheral rod like macrocalcifications. Contrast-enhanced computed tomography (CT) scan showed a right anterolateral mural-based fungating mass lesion, measuring 60× 55 × 60 mm with extra-vesical extension and smudging of the peri-vesical fat planes. The mass spared both vesico-ureteric junctions, both semino-vesical junctions and the prostate. Small peri-vesical prominent enhancing lymph nodes were noted (Fig. 1).

A trans-urethral biopsy was performed, and fragments weighing 2.42 g from the mass with a separate biopsy from the deep muscle weighing 1.13 g were received to the pathology laboratory. Histological examination of both biopsies (Fig. 2) revealed focally ulcerated urothelium with underlying tumor formed of sheets of non-cohesive large malignant epithelioid cells showing marked pleomorphism, hyperchromatic nuclei with bizarre and multinucleated forms. Mitotic activity was marked. Tumor cells were seen embedded in an eosinophilic osteoid matrix with focal calcification. Immunohistochemical study revealed diffuse positive reaction of the tumor cells for

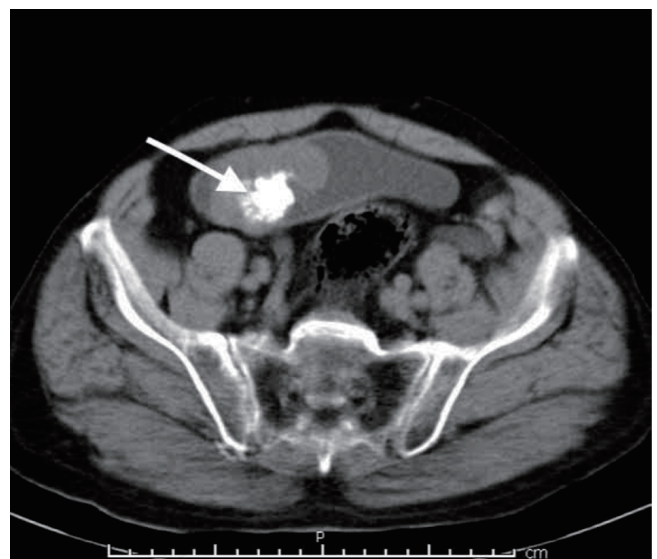


Figure 1. Computed tomography findings of the urinary bladder mass lesion (arrow denotes the tumor).

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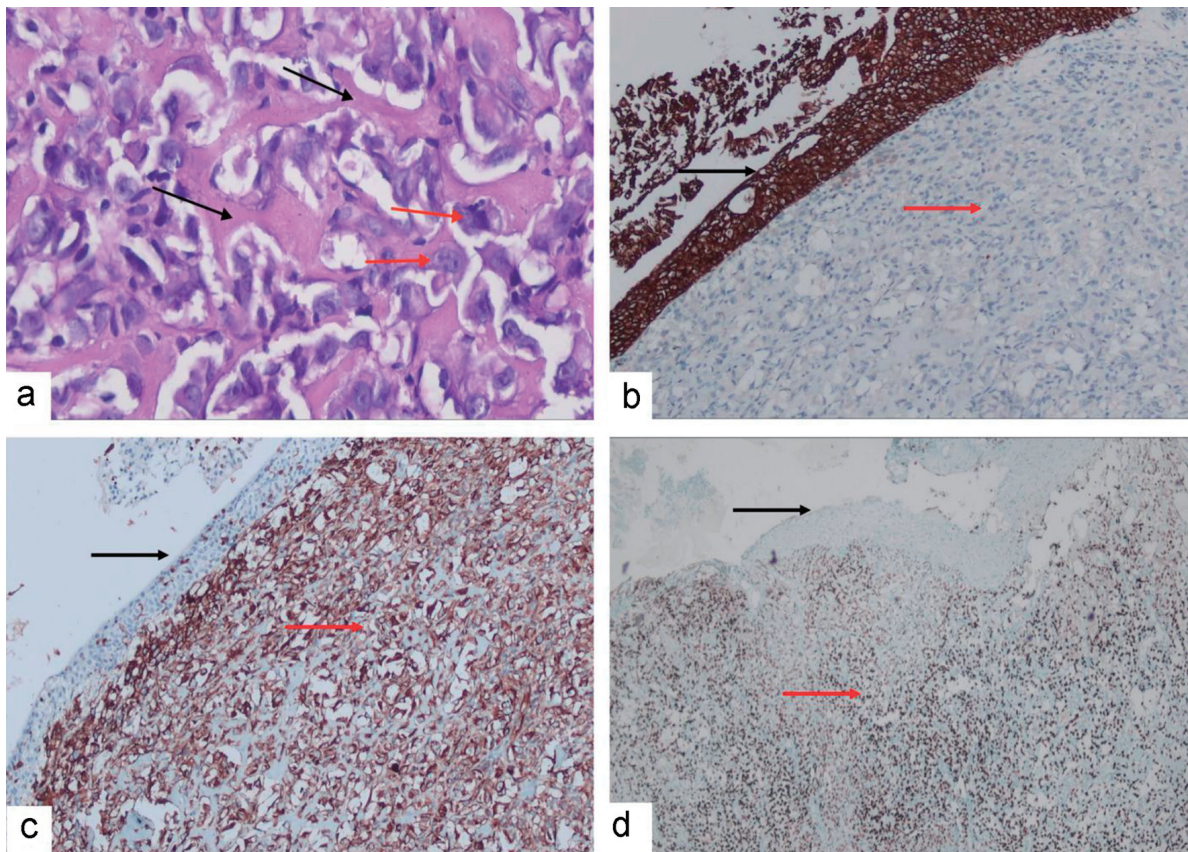


Figure 2. (a) Hematoxylin and eosin-stained sections reveal malignant bone forming neoplasm formed of highly anaplastic cells (red arrows) admixed with abundant lace-like malignant osteoid (black arrows). Immunostained sections reveal that tumor cells are negative for CK (red arrow) which stains the lining urothelium (black arrow) (b). Tumor cells are positive membranous and cytoplasmic immunoreactivity for vimentin (red arrow) which is negative in the surface urothelium (black arrow) (c). Tumor cells (red arrows) show nuclear positivity for SATB-2 (red arrow) which is negative in the surface urothelium (black arrow) (d).

vimentin and SATB-2 but negative for cytokeratin (only stained the residual intact urothelium). The lack of urothelial carcinoma or carcinosarcoma components in our case has qualified the diagnosis of primary osteosarcoma.

The patient received one cycle of cisplatin 60 mg/m² and adriamycin 60 mg/m², and then was admitted to the intensive care unit (ICU) with electrolytes disturbance.

Follow-up chest CT after 1 month revealed multiple bilateral scattered pulmonary nodules, some of which were calcified with the largest noted at the anterior segment of the right upper lobe of lung measuring about 2.5 cm, likely metastatic. The patient lost to follow-up 2 months after diagnosis.

Discussion

ESOS is a rare mesenchymal neoplasm, first described in 1941. It represents 1-2% of all soft tissue sarcomas [1] and 2-5% of all osteosarcomas [3]. Unlike conventional osteosarcoma, ESOS is more frequent among elders [5]. Histologically, ESOS is classified into the same subtypes of the skeletal osteosarcoma [6].

Reported sites involved by ESOS include limbs, retro-

peritoneum, chest wall and breast. In the latter, ESOS is distinguished from matrix-producing carcinomas by the lack of any epithelial component [2]. Primary urinary bladder sarcomas are uncommon and comprise < 1% of all urinary bladder malignancies [7], and osteosarcomas in particular are exceedingly rare [8]. It is more common in males than in females with a male to female ratio of 4:1, and usually presents with hematuria [4, 8].

The main differential diagnosis of urinary bladder ESOS is sarcomatoid carcinoma and urothelial carcinomas with osseous metaplasia [9]. In our case, the histology was identical to conventional bone osteosarcoma with the characteristic lace-like osteoid, calcification and osteoid-related osteoblastic cells of marked pleomorphism. The sections were totally lacking any evidence of an epithelial component. Additionally, the tumor cells were diffusely positive for SATB-2 and vimentin, but negative for CK. However, the distinction from carcinosarcoma does not have major therapeutic implications, as both tumors require aggressive therapy, yet the distinction from low-grade urothelial carcinoma with osseous metaplasia is important [8].

Surgery is the standard of care for management of localized ESOS. The role of systemic chemotherapy remains con-

controversial with no comparative studies conducted due to rarity of disease. The currently available evidence comes from retrospective cohorts with small size.

A case series published in 2005 suggested improved outcome of ESOS patients receiving multi-agent chemotherapy protocols of conventional osteosarcoma for localized disease [10]. Another study suggested superiority of osteosarcoma-type chemotherapy (methotrexate, cisplatin, doxorubicin and ifosfamide) compared to soft tissue sarcoma-type chemotherapy (anthracycline-based +/- ifosfamide chemotherapy) in the perioperative setting [2]. Data on metastatic disease remain very limited.

A trend towards improvement of progression-free survival/overall survival (PFS/OS) was reported in patients receiving platinum-based chemotherapeutic regimens [11]. However, these findings were recently challenged by results of large studies [5, 12].

A retrospective SEER database analysis recently reported including 310 patients presented between 1975 and 2016, making it the largest series up till now [5], showed no specific effect for chemotherapy on prognosis. However, this study included only 51 cases with visceral ESOS. Old age, visceral primary site, no surgical resection and distant metastases were poor prognostic factors [5]. Data on targeted therapy for ESOS are very limited.

Based on the previous data, and due to controversial findings and absence of high-grade evidence, systemic chemotherapy is usually adapted with either a platinum-based combination or osteosarcoma-type chemotherapy [10].

ESOS is a high-grade sarcoma with poor prognosis. In relatively large cohort studies of patients with ESOS, the 5-year OS is less than 50% for localized tumors and less than 30% for metastatic patients [2]. ESOS has a high recurrence rate after resection that reported to be as high as 50% [1, 3]. There are several reported poor prognostic factors that include patient age > 40 years, relatively large tumor size > 5 cm, retroperitoneal and intra-abdominal tumors, positive margins, regional lymph node involvement and distant metastasis [2, 3]. The most common cause of death is distant metastasis, with the lung being the most common site [7].

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Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Author Contributions

Research concept and design: NM. Collection and/or assembly of data: NM, MS, MEK, ASO, MM, YA, ASa. Data analysis and interpretation: NM, MEK. Writing the article: NM, AE, MEK. Preparations of figures and figure legends: AE, MS, ASO, MM, YA, ASa. Critical revision of the article: NM, AE, MS, NR, MEK, ASO, MM, YA, ASa. Final approval of article: NM, AE, MS, NR, MEK, ASO, MM, YA, ASa.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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